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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,775	12/18/2001	Mark David Fidock	PC10959AGPR	6589

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EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/023,775	Applicant(s) FIDOCK, MARK DAVID
	Examiner Ruixiang Li	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *9,11-18,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicants' election with traverse of Group I (claims 1-8, 10, and 19) in Paper No. 10 filed on May 9, 2003 is acknowledged. The traverse is on the grounds (i) that it would not be an undue burden on the Examiner to search all of the claims of this application at once; and (ii) that at least the claims of Groups I and II should be recombined, as it clearly will be necessary to search all of the polypeptide and polynucleotides sequences no matter which group is elected. This has been fully considered but is not deemed to be persuasive for the following reasons. First, Groups I-VI are distinct inventions, it would constitute an undue burden on the office to search and examine all of the groups. Secondly, Groups I and II are drawn to different products, a polynucleotide and a polypeptide. While search of the two groups of invention may have some overlap, each group of invention does require separate search and consideration because the polynucleotides and polypeptides are searched in separate databases and a search of one does not yield comparison with the other. The search and consideration of both groups constitutes an undue search burden on the office, given the ever-increasing size of the database.

   The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-21 are pending. Claims 1-8, 10, and 19 are under consideration. All other claims are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional applications 60/260,590 (filed on 01/09/2001) and 60/296,660 (filed on 06/07/2001).

Acknowledgment is also made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

4. The drawings filed on 12/18/2001 are accepted by the Examiner.

Rejections—35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 5 and 6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 5 and 6 recite a host cell transformed with a vector. Thus, the claims read on a transgenic human, which is non-statutory subject matter. It is recommended that "a host cell" be replaced by "an isolated host cell" to overcome this rejection.

7. Claims 1-8, 10, and 19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-8, 10, and 19 are drawn to an isolated polynucleotide, a vector, a host cell, and a method of producing a polypeptide encoded by the polynucleotide. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention which does not requires further research.

The invention is based upon the discovery of PFI-019 nucleic acid sequence by bioinformatics analysis. The specification asserts that PFI-019 nucleic acid sequence encodes a encoding a G-protein coupled receptor whose ligand is likely to be a nucleotide or a nucleotide derivative and that the PFI-019 polypeptide is most similar to P2Y1 receptor (page 17; Fig. 2). The specification shows PFI-019 polypeptide activation by various purinoceptor agonists in a FLIPR cell-based assay (Example 4; Figures 3-6). Nonetheless, the specification fails to show the specific biological functions or any physiological significance of the PFI-019. It has been well documented that UTP is an inactive agonist for P2Y1 receptor (Harden et al, Annu. Rev. Pharmacol. Toxicol. 35: 541-579, 1995; Ayyanathan et al, BBRC. 218 :783-788, 1996 ; Bhagwat et al, Eur. J. Med. Chem. 32:183-193, 1997; King et al, TIPS, 19 :506-514, 1998 ; Kugelgen etal, Naunyn-schmiedeberg's Arch Phamacol. 362: 310-323, 2000). However, the specification discloses that UTP is a very potent agonist of the polypeptide and is nearly 10 times as potent as 2-methyl-thio-ATP or 2-chloro-ATP (Fig. 3-6). This contradiction clearly indicates that further research is needed to establish the biological functions of the polypeptide of the present invention.

The specification asserts that the present invention provides agonists and antagonists of the polypeptides of the present invention, which are useful in treatment of a list of numerous diseases (pages 6-7 of specification). However, these asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. The specification neither identifies the biological functions of the polypeptides or nucleic acids of the present invention nor any diseases that are associated with the molecules of the present invention. Clearly, further research would be required to determine the functions of the claimed molecules or to identify a disease that can be treated or diagnosed with the claimed molecules See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

The specification further asserts the utilities of polynucleotides as primers or hybridization probes (page 12, 4th paragraph). However, such uses are all considered research uses only designed to identify a particular function of the claimed molecules and are not a substantial utility. See, e.g., *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility." Moreover, such uses are not specific to the instant molecule but applicable to any nucleic acid molecules.

The invention also lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The assertion that the claimed nucleic acid encodes the polypeptide of PFI-019 which is similar to

P2Y receptors (page 17) does not endow the claimed nucleic acids with a specific and substantial utility because members of P2Y receptors have diverse structures and biological functions (see, e.g., Harden et al, Annu. Rev. Pharmacol. Toxicol. 35: 541-579, 1995; Bhagwat et al, Eur. J. Med. Chem. 32:183-193, 1997) and the functions of each P2Y receptor need to be determined individually. No art of record discloses or suggests any property or activity for the claimed molecules such that another non-asserted utility would be well-established for the compounds.

8. Claims 1, 3-8, and 10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, even if the nucleic acid molecule comprising SEQ ID NO: 1 or a polynucleotide encoding the polypeptide of SEQ ID NO: 2 were to have a patentable utility, the instant disclosure would not be found to be enabling for the full scope of the claimed invention.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 1 recites a genus of nucleic acid molecules comprising (i) a

polynucleotide comprising a nucleotide sequence that has at least 75% identity to SEQ ID NO: 1 or a polynucleotide encoding the polypeptide of SEQ ID NO: 2; (ii) a polynucleotide comprising a nucleotide sequence which hybridises to SEQ ID NO: 1 or a polynucleotide encoding the polypeptide of SEQ ID NO: 2; and (iii) a polynucleotide fragment of (i) and (ii). Claims 3-8 and 10 depend upon claim 1.

However, other than the nucleic acid molecule comprising SEQ ID NO: 1 or a polynucleotide encoding the polypeptide of SEQ ID NO: 2, the specification does not provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure does not show (i) which portions of SEQ ID NO: 1 are critical to the activity of the polypeptide encoded by the claimed nucleic acids; and (ii) what modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO: 1 will result in protein mutants with the same functions as the polypeptide of SEQ ID NO: 2. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz, et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein.

Finally, c laim 1 (b) recites NCIMB Deposit No. 41101. Applicants' referral to the NCIMB Deposit No. 41101 on page 14 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have

been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by Applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State.

Accordingly, the disclosure fails to enable such a myriad of the claimed nucleic acid molecules that not only vary substantially in length but also in nucleic acid composition and to provide any guidance to one skilled in the art on how to make and use the claimed genus of nucleic acid molecules. Thus, it would require undue experimentation for one skilled in the art to make and use the claimed genus of the molecules embraced by the instant claims.

Claim Rejections—35 USC § 112, 1st paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-8, and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification discloses a nucleotide sequences set forth in SEQ ID NO: 1, which encode a polypeptide of SEQ ID NO: 2. However, claim 1 as written includes a genus of nucleic acid molecules comprising (i) a polynucleotide comprising a nucleotide sequence that has at least 75% identity to SEQ ID NO: 1 or a polynucleotide encoding the polypeptide of SEQ ID NO: 2; (ii) a polynucleotide comprising a nucleotide sequence which hybridises to SEQ ID NO: 1 or a polynucleotide encoding the polypeptide of SEQ ID NO: 2; and (iii) a polynucleotide fragment of (i) and (ii). Claims 3-8 and 10 depend from claim 1. Thus, the claims encompass a huge number of nucleic acids that vary substantially both in length and in nucleotide composition. In fact, the claims encompass virtually any random nucleic acid sequence of any length because one or two nucleotides can be considered as "a fragment" of a nucleotide sequence and because any nucleic acids could hybridize to SEQ ID NO: 1 or a polynucleotide encoding the polypeptide of SEQ ID NO: 2 since claim 1 (part e) has no recitation of specific hybridization conditions.

The instant disclosure of nucleic acids of SEQ ID NO: 1 that encode the single polypeptide of SEQ ID NO: 2 does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University*

of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed polynucleotides as being identical to those instantly claimed.

Due to the breadth of the claim genus and lack of the definitive structural or functional features of the claimed genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the claimed genus.

Claim Rejections—35 USC § 112, 2nd paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite because it recites "a membrane preparation of the cells". It is unclear whether applicants intend to claim a preparation of the polypeptide of SEQ ID NO: 2 (or its variants) or a membrane preparation that does not necessarily comprise the polypeptide of SEQ ID NO: 2 (or its variants).

Claim Rejections—35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1-8, 10, and 19 are rejected under 35 U.S.C. §102(e) as being anticipated by Wei et al. (Application US/10270144, Publication No. US20030049790A1, pub. Date: March 13, 2003; 102 (e) date: May 18, 2000).

Wei et al. teach an isolated nucleic acid molecule comprising a nucleotide sequence (claim 5) that is 100% identical to the polynucleotide set forth in SEQ ID NO: 1 and encodes a G-protein coupled receptor with the amino acid sequence being 100% identical to SEQ ID NO: 2 or the amino acid sequence of PFI-019 polypeptide encoded by the DNA contained in NCIMB 41101 (see attached sequence alignment). The complement of the nucleic acid molecule taught by Wei et al., by its nature, would hybridize to the nucleic acid molecule. Wei et al. teach the use of polynucleotide with 12 or more contiguous nucleotides as DNA probes and primers (see paragraph [0126]).

Wei et al. further teach a nucleic acid vector comprising the nucleic acid molecule, a host cell containing the vector, and a method for producing the polypeptide (claims 8-11). Since the polypeptide encoded by the nucleic acid

molecule is a GPCR, expression of the polypeptide necessarily results in the expression of the polypeptide at the surface of the host cells (except E. coli in which the majority of the polypeptide would be present in inclusion bodies). A method of producing the polypeptide also necessarily comprises the step of purification of the polypeptide by isolating the membrane of the host cells.

In addition, it is well known in the art to produce a microorganism, such as E. coli., comprising a nucleic acid sequence if the nucleic acid sequence is known as is the case here. In fact, Wei et al. teach a host cell comprising the nucleic acid encoding the polypeptide of PFI-019, which reads the limitation of claim 19. Therefore, the reference of Wei et al. meets the limitations of claims1-8, 10, and 19.

15. The prior art made of record in form PTO-892 and not relied upon is considered pertinent to Applicants' disclosure.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li
Examiner
July 10, 2003

JANET ANDRES
PATENT EXAMINER